Primary Malignant Mixed Müllerian Tumor of the Ovary

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SUMMARY

Objective: To present a case of malignant mixed müllerian tumor of the ovary, a rare and aggressive ovarian malignant tumor with poor prognosis.

Case Report: A 52-year-old woman consulted our outpatient department with complaints of abdominal distention and a firm palpable mass over her lower abdomen. Physical examination and computerized tomography revealed cystic mass lesions on the bilateral adnexal areas. Ovarian cancer was suspected, so the patient underwent exploratory laparotomy. Optimal debulking surgery was performed, and final pathology revealed malignant mixed müllerian tumor of the ovary. Chemotherapy using ifosfamide and cisplatin were administered postoperatively, and adjuvant was also administered. After six cycles of chemotherapy, the patient is well with no signs of recurrence.

Conclusion: Ovarian malignant mixed müllerian tumor usually yields poor outcomes; hence, aggressive treatment with optimal debulking surgery followed by combination chemotherapy using ifosfamide and cisplatin may improve patient outcomes. [*Taiwan J Obstet Gynecol* 2010;49(1):87–90]

Key Words: carcinosarcoma, malignant mixed müllerian tumor, ovary

Introduction

Malignant mixed müllerian tumors (MMMTs) are uncommon neoplasms of the female genital tract that are histologically defined by the presence of malignant epithelial and stromal elements [1]. According to the National Comprehensive Cancer Network clinical practice guidelines in oncology (2008), MMMT is classified as a carcinosarcoma. This type of malignant tumor can arise from any genital organ and occurs mainly in the uterus; however, carcinosarcoma of the ovary is a very rare tumor, which constitutes less than 1% of all ovarian malignancies [2]. Ovarian carcinosarcoma is characterized by aggressive behavior with rapid progression and poor prognosis, with few women with ovarian carcinosarcoma surviving longer than a few years. Optimal debulking surgery followed by chemotherapy is the treatment of choice for this type of malignancy [3].

We report a case of advanced primary ovarian carcinosarcoma, outlining the clinical features, pathologic characteristics, and management.

Case Report

A 52-year-old woman, gravida 3, para 3, who went through menopause at 50 years of age, with no history of hormone therapy or major systemic disease except for tubal ligation and appendectomy in 1979, began to suffer from abdominal discomfort and gastrointestinal upset for about 1 year. She had previously visited a gastroenterologist and taken medications for 3 months without improvement of the symptoms. Shortly beforehand, she had started to complain of abdominal distention and a firm palpable mass over her lower abdomen. The patient was advised to visit a gynecologist for help, but she hesitated and started taking Chinese herbal

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medicine for around 1 month. Unfortunately, enlargement of the mass was noted, and she finally decided to visit our outpatient department.

Physical examination revealed a huge pelvic mass and abdominal tenderness with mild rebounding pain. Pelvic examination revealed a retracted cervix and bilateral adnexal mass. Transvaginal ultrasound was performed showing bilateral pelvic masses approximately 81 × 79 × 94 mm and 72 × 40 × 68 mm in size, with flow and solid components. Malignancy was highly probable, and a computed tomography scan was arranged. This scan revealed a multiloculated low-density lesion with peripheral enhancement about 11.6 × 10 × 18 cm from bilateral adnexa, with superior extension into the abdomen, encasing the ileum and resulting in bilateral hydronephrosis and hydroureter. Ovarian cancer with intraperitoneal seeding was considered. There were no specific findings on upper gastrointestinal endoscopy, colonoscopy, and breast sonography.

Laboratory test results were generally within normal limits except for elevated lactate dehydrogenase (662 U/L), high platelet count (492,000/mm^3), and low hemoglobin (11.1 g/dL). Tumor markers revealed that serum α-fetoprotein was 1.46 ng/mL, carcinoembryonic antigen was 1.44 ng/mL, cancer antigen (CA) 125 was 241 U/mL, CA 153 was 12.32 U/mL, and CA 199 was 17.34 U/mL.

The patient underwent exploratory laparotomy, and huge bilateral ovarian tumors with abdominal carcinomatosis were noted. The tumors involved bilateral ovaries and fallopian tubes, the uterine surface, cul-de-sac, urinary bladder surface, pelvic wall, intestinal wall, mesentery, and omentum. Frozen control tests proved that the mass was malignant, and optimal debulking surgery was performed. Grossly, the bilateral ovarian tumors measured 12 × 8 × 7 cm and 8 × 6 × 4 cm and were brown in color. Dissection of the tumors revealed cystic and solid components with necrosis and hemorrhaging.

Histologically, the ovarian tumors showed a picture consistent with the heterologous variety MMMT composed of an epithelial element and a mesenchymal element. The epithelial element was composed of endometrioid glandular pattern. The mesenchymal element was composed of spindle tumor cells (Figure 1) floating in the cartilaginous matrix. Osteoid matrix formation was also noted. The epithelial element was immunoreactive for cytokeratin (Figure 2), but the mesenchymal element was not. Final diagnosis of primary heterologous ovarian MMMT stage IIIc was given.

Following the debulking surgery, adjuvant chemotherapy using ifosfamide and cisplatin every 3 weeks for six cycles was initiated. Chemotherapy was administered as follows: cisplatin 50 mg/m^2 on day 1 and ifosfamide 1 g/m^2 on day 1, day 2, and day 3 of each cycle. We monitored the status of the disease using tumor marker CA 125 and image studies. Levels of CA 125 decreased to normal range after the first chemotherapy cycle. Follow-up after completion of therapy showed no increase in the tumor marker (Figure 3), and the computed tomography scan did not disclose abdominal recurrence.

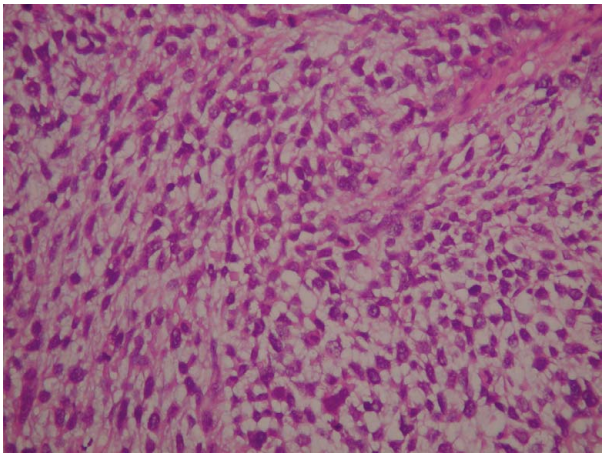

Figure 1. Mesenchymal element composed of spindle tumor cells (hematoxylin and eosin, ×200).

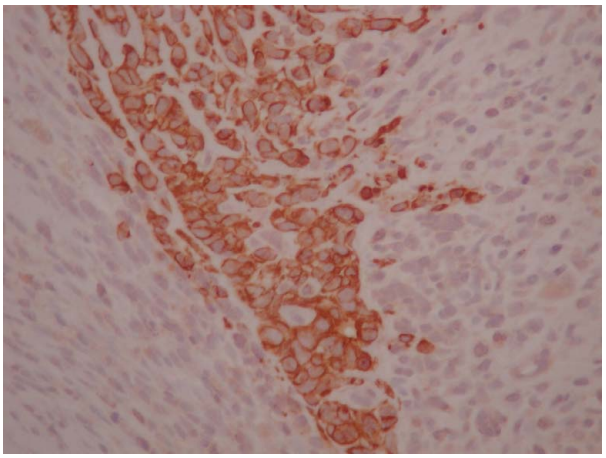

Figure 2. Epithelial element immunoreactive for cytokeratin (cytokeratin stain, ×200).

Discussion

Carcinosarcoma is a biphasic tumor with malignant epithelial and malignant mesenchymal elements. The mesenchymal component usually contains heterologous elements such as cartilage, skeletal muscle, bone, or fat [2,4]. This type of tumor is unusual and only a few cases are reported each year, and these have a tendency to be associated with less favorable outcomes.

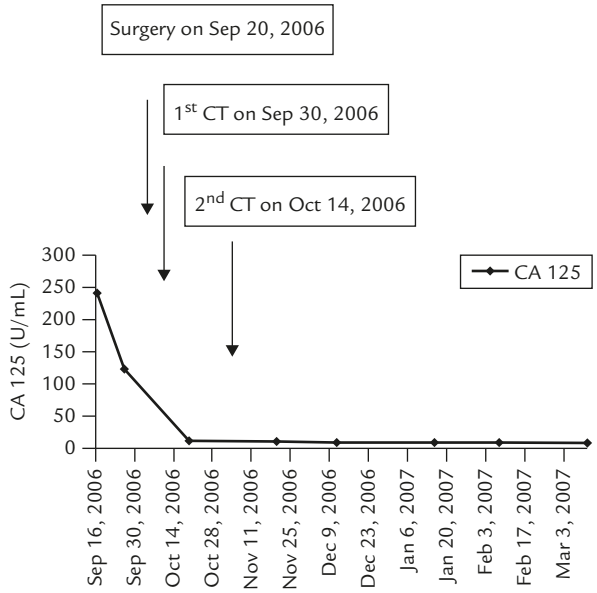

Figure 3. Changes of cancer antigen (CA) 125 level after surgery and chemotherapy (CT).

The majority of patients present with stage III–IV disease, and approximately 75% of reported patients die of the disease in an average of 12 months postoperatively. The histogenesis of carcinosarcoma arising in the ovary remains controversial. Theoretical origins include the müllerian duct, mesoderm, and endometriosis [5].

The most common symptoms and signs of carcinosarcoma of the ovary are abdominal fullness and abdominal mass [6,7]. CA 125 is a highly specific tumor marker for ovarian tumors, especially for serous adenocarcinoma, and it has also been shown to be a useful tumor marker for ovarian carcinosarcoma. Histologically, the cytokeratin immunohistochemical staining is positive in the epithelial element of carcinosarcoma.

Optimal debulking surgery represents the most realistic chance for long-term survival. In a series of studies, the ability to achieve optimal cytoreduction was associated with a statistically significant improvement in survival [8,9]. However, radiotherapy may be appropriate for patients with chemotherapy-refractory recurrent or persistent disease that is restricted to the pelvis [10].

We report this case of primary heterologous carcinosarcoma of the ovary with advanced disease. After optimal debulking surgery, six courses of combination chemotherapy with ifosfamide and cisplatin were initiated and finalized. At the time of writing, the patient had been disease-free for 18 months with regular follow-up examinations at our outpatient department. Ovarian carcinosarcoma is definitely sensitive to platinum compounds [4,11]. In a small non-randomized trial [12], the rate of response to the combination of ifosfamide and cisplatin was 33%. Subsequently, a large phase III trial conducted by the Gynecology Oncology Group compared single-agent ifosfamide [13] with the combination of cisplatin and ifosfamide. Results showed superior activity and only slightly improved progression-free survival with this combination, with no difference in terms of survival and at the cost of increased toxicity. In another study [14], a total of 31 patients underwent initial surgical treatment. Postoperative, neoadjuvant chemotherapy consisted of 16 patients with carboplatin/paclitaxel, 11 patients with ifosfamide/cisplatin, one with cyclophosphamide/doxorubicin/cisplatin, one with carboplatin alone, and two receiving no further treatment. The progression-free survival interval was improved with the use of ifosfamide/cisplatin versus carboplatin/paclitaxel. The overall survival was also significantly improved with the use of ifosfamide/cisplatin ($p = 0.03$). Crotzer et al [15] reported the efficacy and toxicity of cisplatin and ifosfamide in the treatment of patients with MMMT of the ovary, with a response rate of 78% accompanied with a high incidence of adverse effects. In conclusion, the doublet cisplatin/ifosfamide should be the initial treatment for ovarian carcinosarcoma, but higher toxicity should be considered. Novel agents with activity against MMMT of the ovary and acceptable toxicity are, therefore, needed.

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